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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/807,509	06/25/2001	Fritz Grunert	24741-1523	9439
26633	7590	02/23/2005	EXAMINER	
HELLER EHRMAN WHITE & MCAULIFFE LLP 1717 RHODE ISLAND AVE, NO WASHINGTON, DC 20036-3001			WEHBE, ANNE MARIE SABRINA	
			ART UNIT	PAPER NUMBER
			1632	

DATE MAILED: 02/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/807,509

Applicant(s)

GRUNERT ET AL.

Examiner

Anne Marie S. Wehbe

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
 - If no period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 November 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6, 8-12, 15-17 and 19-22 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6, 8-12, 15-17, and 19-22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Applicant's amendment and response received on 11/29/04 has been entered. Claims 1-6, 8-12, 15-17, and 19-22 are pending and under examination in the instant application. An action on the merits follows.

Those sections of Title 35, US code, not included in this action can be found in previous office actions.

Claim Rejections - 35 USC § 112

The rejections of claims 1-6, 8-12, 15-17, and 19-22 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, are withdrawn in view of applicant's amendments to the claims.

Claim Rejections - 35 USC § 103

The rejection of claims 1-6, 8-12, 15-17, and 19-22 under 35 U.S.C. 103(a) as being unpatentable over Forster et al. (1993) Biochem. Biophys. Res. Comm., Vol. 196 (3), 1496-1503, in view of U.S. Patent No. 5,736,524 (4/7/98), hereafter referred to as Content et al., and further in view of Letesson et al. (1997) Clin. Diag. Lab. Immunol., Vol. 4, 556-564 and Whitehorn et

al. (1995) Bio/Technology, Vol. 13, 1215-1219, is maintained. Applicant's arguments have been fully considered but have not been found persuasive in overcoming the instant rejection for reasons of record as discussed in detail below.

The applicant argues that the obviousness rejection is improper because in the opinion of the applicant is rests on hindsight reasoning. The applicant states that the office has not provided a suggestion to make the combination of cited references nor provided a reasonable expectation of success. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the previous office action stated that Forster et al. teaches a method of making antibodies nearly identical to that claimed by the applicants with the exception that Forster et al. teaches the administration of transfected cells expressing the fusion protein to mammals rather

than the direct administration of DNA encoding the fusion protein to generate antibodies. Content et al. was cited to supplement the deficiency in Forster for direct administration of DNA encoding a fusion protein to generate antibodies. As stated in the previous office action, Content et al. teaches the generation of antibodies *in vivo* in mice by direct administration of a DNA plasmid vector encoding a polypeptide of interest. Further, Content et al. provides motivation to use eukaryotic vectors instead of protein to generate antigen specific antibodies *in vivo*. Content teaches that its better to immunize with a gene rather than a gene product for the following reasons: 1) the simplicity with which native or nearly native antigen can be presented to the immune system using genetic immunization, and 2) the fact that mammalian proteins expressed recombinantly in bacteria, yeast, or even mammalian cells often require extensive treatment to insure appropriate antigenicity (column 9, lines 60-66). Thus, the rejection of record clearly indicates that Content et al. provides the specific suggestion to use direct gene delivery *in vivo* rather than protein or cell delivery to generate antibodies against that protein. In view of the motivation provided by Content et al. to use a gene rather than a gene product or cell to produce antibodies *in vivo*, the previous office action concluded that it would have been *prima facie* obvious to the skilled artisan at the time of filing to directly inject the expression vector encoding the fusion protein taught by Forster et al. *in vivo* rather than the cells transfected with the expression vector to produce antibodies.

In regards to the combination of Letesson et al. or Whitehorn et al. with Content et al. and Forster et al., the previous office action pointed out that while the primary reference, Forster et al., teaches the use of a myc tag as a detection/purification signal, Forster et al. does not specifically teach the use of other types of detection signals such as hexa-histidine or GPI

residues. Therefore, the rejection supplements the teachings of Forster et al. with those of Letesson et al. and Whitehorn et al. which teach that at the time of filing, it was standard technique to use various epitope tags to detect fusion protein expression, and to use fusion proteins containing MYC, hexahistidine tags, or GPI residues, in immunoassays. Using the standard set forth in *In re Fine* and *In re Jones* that motivation to combine the teaching of references can be found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, the office found that based on the teachings in the cited art that various epitope tags can be successfully used to detect fusion protein expression, and in particular, the MYC epitope tag, hexahistidine tags, or GPI residues, the skilled artisan would have been motivated to substitute other well-known detection signals such as hexahistidine or GPI for MYC in the methods of making and using fusion proteins taught by Forster et al. in view of Content. Further, based on the high level of skill in molecular biology as exemplified in the teachings of the cited references, the skilled artisan would have had a reasonable expectation of success in modifying the vector taught by Forster et al. to include a hexahistidine epitope tag or a GPI tag. Thus, as demonstrated above, the rejection of record clearly identified the motivation to combine the teachings of the references cited and showed that the skilled artisan would have had a reasonable expectation of success in combining their teachings as indicated.

The applicant further argues that Content et al., Letesson et al., and Whitehorn et al., describe "old elements" or techniques that are well-known in the art and states that the examiner has done little more than cite references to show that the various parts were known in the art. Applicant's characterization of the rejection of record is not agreed. As discussed in detail above,

the rejection of record clearly points of the teachings of the primary reference, Forster et al., and provides specific motivation for why the skilled artisan would combine the teachings of Content et al., Letesson et al., and Whitehorn et al. with Forster. Further, it is unclear what applicant means by "old elements". If the applicant is commenting on the age of the references, the applicant is reminded that contentions that the references are old are not impressive absent a showing that the art tried and failed to solve the same problem notwithstanding its presumed knowledge of the references. See *In re Wright*, 569 F.2d 1124, 193 USPQ 332 (CCPA 1977).

The applicant further states that the teachings of Content et al., Letesson et al., and Whitehorn et al. are not directed to methods of producing and screening antibodies as claimed. In response, the primary reference, Forster et al., discloses just such methods, the teachings of the secondary references are used to supplement the teachings of Forster et al. Finally, please note that the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). Therefore, for the reasons of record as discussed in detail above, the rejection of record is maintained.

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. The examiner can be reached Monday- Friday from 9:30-6:00 EST. If the examiner is not available, the examiner's supervisor, Ram Shukla, can be reached at (571) 272-0735. For all official communications, **the new technology center fax number is (571) 273-8300**. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737.

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER

